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| 09/769,107 | 01/24/2001 | Vincent P. Sandanayaka | AM-100182 01 | 4495 |
| 25291 | 7590 | 09/21/2005 | EXAMINER | |
| WYETH PATENT LAW GROUP 5 GIRALDA FARMS MADISON, NJ 07940 | | | COVINGTON, RAYMOND K | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1625 | |

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/769,107

Applicant(s)

SANDANAYAKA ET AL.

Examiner

Raymond Covington

Art Unit

1625

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION:

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 July 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14,29-31,33-39 and 45-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-14,29-31,33-39 is/are allowed.
- 6) ☒ Claim(s) 45-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

GA

Regarding the office action of September 24, 2003 the period for response was reset on October 25, 2004.

Regarding the Restriction requirement and election of species, election of Group I claims 1-14 with the election of species of example 36 is noted. Claims 29-31 and 33-39 are included with the Group I election. Likewise, claims 45-47 is also grouped with the elected invention.

Accordingly, claims 1-14, 29-31, 33-39, 45-47 and 53 are examined as the Group I election.

Upon reconsideration pursuant to Rejoinder practice, claims 48-52 upon determination of allowable subject matter will be rejoined and considered with the elected invention.

Claims 1-14, 29-31, 33-39, 45-47 and 53 are allowed. The prior art does not teach or suggest alpha-sulfonyl compounds of formula V where R_1 and R_2 of formula V form a ring or a method of preparing them in the manner set forth in the recited claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 48-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Please note that, claims 48-52 encompass a method of use, which includes those conditions for which its relationship with TACE and matrix metalloproteinases has not been, identified yet i.e. future discovery. In addition, claims 49, 51 and 52 encompassed all cardiovascular disorder, allergic disorder...etc. which are not TACE and matrix metalloproteinases effective and lack enabling support from the specification as to the efficacy of compounds described in claim 1 being useful for such treatment.

Further note that claims 48-52 are drawn to treating and "incredible" kind and number of disorders or conditions for TACE and matrix metalloproteinases activity is not required. In addition, just because TACE and matrix metalloproteinases is involved in pathophysiology is not any indication for the instant compounds being enabled in treating TACE and matrix metalloproteinases "involved" diseases.

Claims 48-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The instant specification does not adequately describe the nexus between TACE and matrix metalloproteinases and a useful treatment of a disease/condition. Modulation of a receptor involves antagonism, inhibition, agonism and others. These modulations are sometimes opposite reactions to the same receptor. It is not seen where the instant specification adequately describes the nexus between the modulation of TACE and matrix metalloproteinases and a useful treatment of a single disease or condition.

Claims 48-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention: The nature of the invention is the method of treating a disorder that is modulated by TACE and matrix metalloproteinases.

The state of the prior art: The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In *re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects of all diseases, whether or not TACE and matrix metalloproteinases would make a difference in the disease. Hence, in the absence of a showing of a nexus between any and all known diseases and TACE and matrix metalloproteinases, one of ordinary

skill in the art is unable to fully predict possible results from the administration of the compound of claim 1.

The amount of direction or guidance present: Pages 1-3 of the specification state that TACE and matrix metalloproteinases is thought to play an important role in a variety of inflammatory diseases and pain. The specification does not seem to enable a correlation between the TACE and matrix metalloproteinases and the treatment of any and all diseases.

The breadth of the claims: The claims are drawn to the treatment of any and all diseases mediated by TACE and matrix metalloproteinases with the compounds of claim 1.

The quantity of experimentation needed: The quantity of experimentation needed is undue. One skilled in the art would need to determine what diseases out of all known diseases would be benefited by the mediation of TACE and matrix metalloproteinases and then would further need to determine which of the claimed compounds would provide treatment of the disease.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which

compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compounds of claim 1 for the treatment of any disease. As a result necessitating one of ordinary skill to perform an exhaustive search for which diseases can be treated by which compound of claim 1 in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds of the instant claims, with no assurance of success.

This rejection can be overcome by deleting the claims.

Claim 49 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention: The nature of the invention is the method of treating HIV.

The state of the prior art: The state of the prior art is that it involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease). There is no absolute predictability and no established correlation between in vitro activity and the treatment of viral conditions such as HIV as the in vitro data is not a reliable predictor of success even in view of the seemingly high level of skill in the art. The existence of these obstacles

establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The predictability in the art: It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In *re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

It is well known in the art that HIV is composed of many different diseases including pneumonia, Kaposi's sarcoma, Epstein Barr virus and various other opportunistic diseases caused by fungi, viruses, bacteria and protozoans. See, for example, *Acta Microbiol. Immun. Hung.* 41(1), 5-21 (1994), *Proc. Annu. Meet. Med. Sect. Am. Counc. Life Insurance*, 41-52 (1993). By using the term HIV treatment of humans in the claim language, applicants are necessarily extending the treatment to these complications against which the invented compounds (or compositions) have not been demonstrated to be effective.

In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would not recognize the nexus between the between in vitro activity and the particular respiratory disease to be treated. Neither

does the instant specification adequately describe the nexus between the between in vitro activity and the treatment of viral conditions such as HIV. Hence, in the absence of a showing of a nexus between any and all known diseases and TACE and matrix metalloproteinases, one of ordinary skill in the art is unable to fully predict possible results from the administration of the compound of claim 1 due to the unpredictability of the role of TACE and matrix metalloproteinases.

The presence or absence of working examples: In addition, there is no proof that the claimed compounds or compositions have ever been administered to a human or to an animal model. The obstacles to therapeutic approaches and vaccine development with regard to retroviruses associated with AIDS in humans are well documented in the literature. See, for example, Huff {J. Med. Chem. 34(8) 1991, p. 2305-2314} on page 2314. These obstacles include and are not limited to: 1) the extensive genomic diversity associated with HIV, particularly with respect to the gene encoding the envelope protein, 2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a convert form, as well as via free virus transmission, 3) existence of a latent form of the virus, 4) the ability

of the retrovirus to traverse the blood brain barrier and 5) the complexity and variation of the elaboration of the disease.

There are insufficient exemplifications to support the treatment of all known respiratory diseases.

The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any vaccine or immunization treatment or any therapeutic regimen on its face. In order to provide proof of utility with regard to drugs and their uses, either clinical in vivo or in vitro data correlative to in vivo applicability or a combination of these can be used. However, the data must be such as to convince one of ordinary skill in the art that the proposed utility is sufficiently established as set forth in full, clear and exact terms in the disclosure. When the utility is directed to humans, the data must generally be clinical, however, adequate animal data would be acceptable in those instances wherein one of ordinary skill in the art would accept correlation to human utility. Thus, in order to rely on animal data, there must exist an art recognized animal model for testing purposes. In re Hartop, 311 F.2d 249, 135 USPQ 419 (CCPA 1962).

The amount of direction or guidance present: There is no proof that the claimed compounds or compositions have ever been administered to a human or to an animal model. The obstacles to therapeutic approaches and vaccine development with regard to retroviruses associated with AIDS in humans are well documented in the literature. See, for example, Huff {J. Med. Chem. 34(8) 1991, p. 2305-2314} on page 2314. These obstacles include and are not limited to: 1) the extensive genomic diversity associated with HIV, particularly with respect to the gene encoding the envelope protein, 2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a convert form, as well as via free virus transmission, 3) existence of a latent form of the virus, 4) the ability of the retrovirus to traverse the blood brain barrier and 5) the complexity and variation of the elaboration of the disease.

The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any vaccine or immunization treatment or any therapeutic regimen on its face. In addition, there is no established correlation between in vitro activity and accomplishing treatment of viral infections, especially HIV infections, in vivo, and those skilled in the art would not accept allegations in

the instant specification, or the in vitro data to be reliable predictors of success, and those skilled in the art would not be able to use the claimed compounds and compositions since there is no description of an actual method wherein a viral infection in a host is treated.

The breadth of the claims: The claims are drawn to the treatment of any and all conditions and diseases mediated by TACE and matrix metalloproteinases.

The quantity of experimentation needed: The quantity of experimentation needed is undue. One skilled in the art would need to determine what HIV and respiratory diseases out of all such known diseases would be benefited by the compounds of claim 1 and then would further need to determine which of the claimed compounds would provide treatment of the disease.

The level of the skill in the art: The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad method recited in applicants' claims. As a result necessitating one of ordinary skill to

perform an exhaustive search for which diseases can be treated by which compound in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, one of ordinary skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compounds of the instant claims, with no assurance of success.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Raymond Covington whose telephone number is (571) 272-0681. The examiner can normally be reached on M-F.


If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, C. Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



RKC

Raymond Covington
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